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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/717,993	11/20/2003	Chi Li Liu	2027.631000	7643

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WILLIAMS, MORGAN & AMERSON
10333 RICHMOND, SUITE 1100
HOUSTON, TX 77042

EXAMINER

MEAH, MOHAMMAD Y

ART UNIT	PAPER NUMBER
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1652

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/717,993

Applicant(s)

LIU ET AL.

Examiner

Mohammad Meah

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 29 November 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 2-23, 102 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Claims 1-23 and 102 were examined in the previous action. With supplemental amendment of this application, the applicant, on date 11/29/06 amended claims 1, 8 and 102.

Claim Rejections

35 U.S.C 112

35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Rejection of claims 1, 2-23 (dependent on claim 1) and 102 are rejected under U.S.C. 112, 2nd paragraph, as explained in the prior action because, recitation of "essentially no ethanol" makes the claim indefinite is maintained. Applicants argument against 112 second paragraph rejection, described on their amendment page 6, is considered but not found persuasive for following reasons. Applicants argue that "essentially no ethanol " is definite. Applicant argue that skilled artisan understand the term "essentially no ethanol " means undetectable amount (including zero amount) of ethanol. The term "undetectable" renders the definition of "essentially no ethanol " indefinite because what is "detectable" depends on the method used and changes with the development of new techniques. The skilled artisan would not know the metes and bounds of the recited invention. It is suggested that "essentially no ethanol " be amended to "no ethanol ".

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Written Description requirement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

As described in the prior action, Claims 1-10, 12-20, 22-23 and 102 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1-8, 12-20, 22-23 and 102 are directed to methods of producing lactic acid comprising using any acid-tolerant (AT) yeast expressing with any exogenous Lactose dehydrogenase (LDH) gene from any source and claims 9-10 are directed to methods of producing lactic acid comprising using acid-tolerant (AT) yeast of *Saccharomyces or candida*, *Kluyveromyces* types expressing any exogenous Lactose dehydrogenase (LDH) gene. The specification teaches method of preparation of lactic acid using a few modified AT yeast strains NRRL-Y-30696, NRRL-Y-30697 or NRRL-Y-30698, which do not represent all AT yeast strains recited in the instant claims. Specification neither teach the structures of all LDH genes nor teach how all AT yeast strain will be modified with all LDH genes. Moreover, the specification fails to describe any other representative species of AT yeast strain by any identifying characteristics or properties other than the acid

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tolerant LDH activity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicants arguments at page 7 of their amendment against rejection of claims 1-10, 12-20, 22-23 and 102 under 35 U.S.C. 112, first paragraph written description are acknowledged but is not found persuasive because these claims still are directed to methods of producing lactic acid comprising using any acid-tolerant (AT) yeast expressing with any exogenous Lactose dehydrogenase (LDH) gene from any source. Therefore, as explain above one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed. Applicants argue that the rejection of claims under 35 U.S.C. §112, first paragraph is not proper because specification teach methods of producing lactic acid comprising the **acid tolerant strain that capable of growing in minimum medium which is apart from any wild type yeast strains** and therefore define the specific genera that skilled artisan can recognize that applicants posses the claimed invention.

Though yeast is known in art for a long time and skilled artisan can modify yeast strain if **structure of recombinant gene is known** to yield desired yeast strain (say acid tolerant, etc), a skilled artisan can not modify any yeast strain with **any gene with any structure** because such genus of gene of having no structural limitation comprise enormous number of genes encoding many LDH

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proteins with unlimited variation in their amino acid sequences that one skilled in the art cannot reasonably conclude that the applicant had not possession of the claimed invention at the time the instant application was filed.

III. Enablement requirement

The following is a quotation of the first paragraph of 35 U.S.C. 112: The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

As described in the prior action, Claims 1-10, 12-23 and 102 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of producing lactic acid comprising using acid- tolerant (AT) yeast strain of NRRL-Y-30696, NRRL-Y-30697 or NRRL-Y-30698 expressing an exogenous Lactose dehydrogenase (LDH) gene from *Lactobacillus plantarum* in plasmid YEpLDH, does not reasonably provide enablement for methods of producing lactic acid comprising using any acid- tolerant (AT) yeast strain expressing any exogenous Lactose dehydrogenase (LDH) gene. The claims broadly recite the methods of producing lactic acid comprising using any acid- tolerant (AT) yeast strain expressing any exogenous Lactose dehydrogenase (LDH) gene. The specification fails to describe how any acid- tolerant (AT) yeast strain expressing any exogenous Lactose dehydrogenase (LDH) gene can produce lactic acid and fails to teach how to make nucleic acids encoding any LDH as needed to practice the scope of the claimed methods.

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Applicants arguments, on page 8-9 of their amendment, against rejection of claims 1-10, 12-23 and 102 under 35 U.S.C 112, first paragraph enablement are acknowledged. Applicants argue that the claims are enabled because specification has given six examples of known LDH genes with SEQ ID NO from *Lactobacillus*, bovine and *Rizopus oryzae*. Therefore; with the knowledge of these structures and the knowledge of LDH activity skilled artisan is enabled to identify any LDH gene from same or any other organisms encoding LDH. These are not found persuasive because claims recite methods of producing lactic acid comprising using **any acid- tolerant (AT) yeast strain expressing any exogenous Lactose dehydrogenase (LDH) gene with any structure (which include enormous amount of genes with variation of any nucleotide residues in any DNA sequence encoding any LDH protein)**. Applicants assertions that, based on known six sequences of LDH gene that applicant described in the specification and common knowledge of molecular biology, a skilled artisan can use applicant's **any unstructured LDH gene** to enable applicant's invention. It is not found persuasive because while methods of expression exogenous gene of known sequence is well known to the skilled artisan, expression of any exogenous gene of recited genus of sequence (i.e., encoding any LDH enzymes) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the enormous numbers of DNAs have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute **undue** experimentation.

Therefore, as explained in the previous office action and **explained below** the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, make and for use the invention commensurate in scope with these claims.

Applicants argue that a skilled person does not require an undue experimentation to make and use the invention. It is not found persuasive because specification does not support the broad scope of the claims, which encompass **any** acid- tolerant (AT) yeast strain expressing any exogenous Lactose dehydrogenase (LDH) gene with any structure. Although specification does teach a few specific DNA encoding a few specific **LDH** proteins be expressed into a host cell so that host cell produce Lactic acid at low pH, it does not describe how to make all those generic genes (having any polynucleotide sequences) encompassed by the instant claims. While methods of producing exogenous gene(s) of known sequence(s) is(are) well known to the skilled artisan. Production of any exogenous gene(s) of genus of sequence(s) as claimed by applicants (i.e., encoding any LDH enzymes) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the enormous numbers of DNAs have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute **undue** experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the

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specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification.

CLAIM Rejection - 35 U.S.C 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless

e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Rejection of claims 1-9, 12-23, 102 under 35 U.S.C. 102(e) as being anticipated by Hause et al. (US 2003/0228671) for the reasons explained in the prior action, is maintained:

Hause et al. teach various recombinant yeasts (*Sachharomyces*, *Kluyvermyces*, *Candida*, etc) which produce high yield of lactic acid (95 gm/ 100 gram of glucose) at low pH (bellow ~2.3) in a culture medium containing at least among others glucose and one nitrogen source, wherein said yeast expresses (through integration to yeast chromosome or through plasmid) various exogenous LDH genes including *from Lactobacillus plantarum*. They also teach the production and isolation of lactic acid at high yield (i.e. 95% or 95gm/ gm of sugar used) without producing any pyruvate at low pH (bellow ~

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2.3) using nitrogen as nutrient and carbohydrate (glucose, etc) as only carbon source.

Applicants argue that Hause et al. only list *Sachharomyces* at paragraph 0067 and since same paragraph recites "Yeast cells that do not accumulate pyruvate, i. e, that naturally metabolize pyruvate to ethanol is preferred," Hause teach way from present claims. This is not found persuasive because 1st of all Hause et al. do not teach use of *Sachharomyces* but use of *Sachharomyces* from which *pdc* gene is deleted and *Sachharomyces* having no *pdc* gene does not produce ethanol (see paragraph 62). 2nd of all Hause et al. state these strains with respect to the expression of exogenous LDH gene. Although Hause et al do not use *Sachharomyces* in their working examples, one of these strains mentioned in paragraph 0067 that applicant alleged teach away, *Kluyveromyces Marxianus* was used for the production of lactate at pH 2.3 wherein no ethanol is produced. Applicant's argument, that Hause et al. does not teach minimal medium and aerobic condition in the process of production of Lactic acid is also not true. Although Hause et al. used variety of harvesting media they also teach a media with only carbohydrate as carbon source and nutrients (nitrogen, minerals etc (page 0075) and also teach fermentation condition with controlled oxygen (aerobic) supply.

Rejection of claim 10 under 35 U.S.C. 102(b) as being anticipated by Hause et al. (US 2003/0228671) is withdrawn after applicants argument.

Claims 1-10, 12-23, 102 are rejected under 35 U.S.C. 102(e) as being anticipated by Rajgarhia et al. (US 2004/0029238). Rajgarhia et al. teach various

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recombinant yeast (*Sachharomyces*, *Kluyvermyces*, *Candida*, etc) strains expressing (through integration to yeast chromosome or through plasmid) various exogenous LDH genes including from *K. lactis*. which capable of growing in minimal medium of cell culture. Rajgarhia et al. also teach method of production of lactic acid (95 gm/ 100 gram of glucose) wherein no ethanol is produced using said yeast strain comprising fermentation step at low pH (bellow ~2.3) in **minimal medium**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR

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system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mohammad Younus Meah, PhD

Examiner, Art Unit 1652

Recombinant Enzymes, 3C31 Remsen Bld

400 Dulany Street, Alexandria, VA 22314

Telephone: 517-272-1261

Rebecca E. Prouty
REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP 1800
1600